Start of Edmund Klein Collection

AR 11687

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LEO BAECK INSTITUTE
Center for Jewish History
15 West 16th Street
New York, NY 10011

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AR 11687 1/1 Edmund Klein Collection 1938-1999 Archives

AHC 712

712

THE AUSTRIAN HERITAGE COLLECTION AT THE LEO BAECK INSTITUTE

AUSTRIAN-JEWISH IMMIGRANTS IN THE USA

LEO BAECK INSTITUTE: 15 WEST 16TH STREET, 4TH FLOOR, NEW YORK, NY 10011, TEL (212) 744 - 6400

Name: Klein (deceased 1999) Edmund

[redacted]

Date of Birth: Oct. 22 1921 **Place of Birth:** Vienna Austria
Month Day Year City Country

Prewar Address: _____
Street (District, if in Vienna) City Country

Prewar Name: Same **Maiden Name:** _____

1. Education/Occupation(s) *(please if possible, indicate institutions and year when entered/left)*
See attached information

2. Were you affiliated with any kind of organization (Youth, Zionist, Political, etc.)? If so, did you have any specific function?
unknown

3. Were you arrested and/or interned? *(please indicate where and when)*
My husband was interned in Canada From 1941 until, I think, the end of the war!

4. What was your route of emigration? *(please indicate places and dates of stay)*
He left Vienna - by train - and ended up in England - from there, he was sent to Canada

5. May we contact you again with a more detailed follow-up questionnaire? *(please circle)* (Yes) / No

6. Do you have any documents, such as photographs, letters, diaries, all kinds of manuscripts, etc., that would be appropriate for the archives of the LBI? (Yes) / No

If necessary please use additional sheets. Thank you!

Edmund Klein Collection (AHC 712)

All documents are copies as otherwise indicated

1. AHC Questionnaire 1

2. List of Awards, education, trainings Mr. Klein received, and furthermore, affiliations with hospitals, short descriptions of research experiments and essays he worked on, (33 pages)

3. Clearance certificate ('Fuehrungszeugnis') for Edmund Klein from the Viennese Police, Vienna 03/12/1957 (1 page, original)

4. Letter from the "Isralitische Kultusgemeinde Wien" to the German Aid Committee, concerning Edmund Klein's ambition to continue his studies in London, Vienna 08/08/1938, (1 page)

5. Portrait of Edmund Klein, by the Journal of Medicine, Vol. 30, NOS. 5 & 6, 1999, (4 pages)

6. Portrait of Edmund Klein, "In Memoriam: Edmund Klein (1921-1999), taken from a magazine, (2 pages, original)

AMTS-DIREKTION
DER
ISRAELITISCHEN KULTUSGEMEINDE
WIEN

WIEN, 8. August 1938.
I. SEITENSTETTENGASSE 4

N-1000

An das

German Aid Committee,

W.C. 1, Woburn House,
Upper Woburn Place.
London.

Der Sohn eines langjährigen Angestellten der Kultusgemeinde, Edmund K l e i n, wird bei Ihnen vorstellig werden.

Der junge Mann will seine Studien in London fortsetzen und verdient jede Förderung.

Ich bitte Sie, ihm an die Hand zu gehen.

Mit vorzüglicher Hochachtung
Der Amtsdirektor:

Leiter der Israelitischen
Kultusgemeinde Wien.

Bundes-Polizeidirektion Wien № 145968

Korrespondenzbüro

K. B. 597/56(A) F. Z. Wien, am 12. März 1957

Verwaltungsabgabe
von 4.- S entrichtet.

Führungszeugnis

Dem ~~(Der)~~ Herrn Edmund K l e i n Beruf: ---

am 22. Oktober 1921 in Wien geboren,

Staatsbürgerschaft Canada

gewesen
wohnhaft/in Wien IX., Türkenstrasse 17

wird zum Zwecke der Vorlage bei Behörden in U.S.A.

während des hiesigen Aufenthaltes

hiemit bestätigt, daß gegen ihn ~~sie~~ Nachteiliges nicht vorgemerkt ist.

(Wiesenberger)

Lager Nr. 36. – Amtsdruckerei der Bundes-Polizeidirektion Wien.

EDMUND KLEIN

EDUCATION

University College, University of Toronto, Canada
Honor Course in Physiology and Biochemistry
B.A., 1947 — 1943-1947

Faculty of Medicine, University of Toronto
M.D., 1951 — 1947-1951

University Laboratory for Physical Chemistry, Harvard University, Research Fellow (Fellowship in Medical Sciences, National Research Council) — 1951-1952

Children's Cancer Research Foundation, Children's medical Center Boston, Mass. Research Fellow, (Fellowship in Medical Sciences, National Research Council) — 1952-1953

PROFESSIONAL TRAINING

Research Associate, Children's Cancer Research Foundation, Department of Dermatology and Clinical Laboratories, Children's Medical Center, Boston, Mass. — 1953-1958

Clinical and Research Fellow, Department of Dermatology, Harvard Medical School and Massachusetts General Hospital, Boston, Mass. — 1956-1958

Assistant Resident, Department of Dermatology, Massachusetts General Hospital, Boston, Mass. — 1958-1959

ACADEMIC AWARDS

Laser Award for Pioneering Contributions in Laser Medicine and Surgery
The International Society of Laser Medicine and Surgery — 1986

Founders Award in Cancer Immunology — 1975

Albert Lasker Award for Clinical Research in Cancer Immunology — 1972

First Prize for Originality of Research from the International Society for Hematology — 1956

AOA Medical Honor Society — 1949

Thirty-six Scholarships for academic proficiency and other miscellaneous awards

ACADEMIC AFFILIATIONS

Teaching Fellow, Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston, Mass.	1958-1959
Research Associate, Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston, Mass.	1959-1960
Assistant Professor, Department of Medicine and Department of Dermatology, Tufts Univeristy School of Medicine, Boston, Mass.	1959-1961
Chief, Department of Dermatology, Roswell Park Memorial Institute Buffalo, New York	1961-1975
Research Professor of Experimental Pathology, State University of New York at Buffalo, Buffalo, New York	1962-
Guest Professor of Biomedical Engineering, Northeastern University Boston, Mass.	1965-
Member, The Center for Immunology, State University of New York at Buffalo, Buffalo, New York	1970-
Research Professor of Medicine (Dermatology), State University of New York at Buffalo, Buffalo, New York	1970-1972
Research Professor of Medicine, State University of New York at Buffalo, Buffalo, New York	1972-
Associate Chief, Department of Dermatology, Roswell Park Memorial Institute, Buffalo, New York	1975-1982

CURRENT AND PREVIOUS CONSULTATIVE APPOINTMENTS

Consultant, Sidney Farber Cancer Center and Children's Medical Center, Harvard Medical School, Boston, Mass.

Member, National Advisory Council on Health Care Technology, the United States Department of Health, Education, and Welfare, Washington, D.C.

Children's Cancer Research Foundation, Children's Medical Center, Boston, Mass.

Acute Leukemia Task Force, National Cancer Institute, United States Department of Health, Education, and Welfare, Washington, D.C.

Advisory Committee on the Biologic Effects of Optical Masers, United States Army Medical Research and Development Command, Office of the Surgeon General, Washington, D.C.

Consultant, Viral Carcinogenesis Branch, Division of Cancer Cause and Prevention, Viral Oncology, National Cancer Institute, Bethesda, M.D.

Chairman, Viral Oncology, Review Committee B, Cancer Cause and Prevention Viral Oncology, National Cancer Institute, Bethesda, M.D.

HOSPITAL AFFILIATIONS		PERIOD
Children's Medical Center Harvard Medical School, Boston, Mass.	Associate, Tumor Therapy Service	1954-1956
Children's Medical Center, Harvard Medical School, Boston, Mass.	Assistant, Clinical Pathology	1954-1956
Massachusetts General Hospital, Harvard Medical School Boston, Mass.	Clinical and Research Fellow in Dermatology	1956-1959
Massachusetts General Hospital Boston, Mass.	Assistant Resident, Dept. of Dermatology	1957-1959
Massachusetts General Hospital and Harvard Medical School, Boston, Mass.	Teaching Fellow, Dept. of Dermatology	1958-1959
Boston City Hospital and Boston Dispensary, Tufts University School of Medicine, Boston, Mass.	Assistant Physician Dept. of Dermatology	1959-1961
Sidney Farber Cancer Center Harvard Medical School Affiliated Hospitals Boston, Mass.	Consulting Medical Staff	1961-1975
Roswell Park Memorial Institute Buffalo, N.Y.	Chief, Dept. of Dermatology	1961-1975
Roswell Park Memorial Institute Buffalo, N.Y.	Associate Chief, Dept. of Dermatology	1975-1983
Roswell Park Memorial Institute Buffalo, N.Y.	Consultant	1983-
Millard Fillmore Hospital Buffalo, N.Y.	Medical Staff	1975-
Sisters of Charity Hospital Buffalo, N.Y.	Courtesy Staff	1975-
Sidney Farber Cancer Center Harvard Medical School Affiliated Hospitals Boston, Mass.	Chief, Skin Cancer Clinic	1975-1980

RESEARCH EXPERIENCE

Nature of Work	Department	Head of Department	Period
Fungicidal action of quarternary ammonium compounds	Plant Physiology Univ. of Toronto	Dr. G.H. Duff	1944-1946
Effects of choline deficiency on tissue lipases	Physiology-Banting and Best Inst. for Medical Research University of Toronto	Dr. C.H. Best	1946-1948
Synthesis of analogues of thyroxine	Organic Chemistry University of Toronto	Dr. C.F. Wright	1947-1949
Metabolic activities of thyroxine analogues	Dept. of Pharmacology, University of Toronto	Dr. J.K.W. Ferguson	1948-1950
Protein-metal interaction in relation to phagocytosis	Univ. Laboratories for Physical Chemistry, Harvard University	Dr. E.J. Cohn	1951-1952
Platelets and WNC preparations in Pancytopenia	Children's Cancer Research Foundation, Children's Medical Center, Boston, Mass.	Dr. S. Farber	1953-1956
Lipoprotein metabolism and transport in hypercholesteremia and hyperlipemia	Dept. of Dermatology Harvard Medical School & Massachusetts General Hospital	Dr. M.M. Tolman Dr. W.F. Lever	1956-1960
Lipoprotein metabolism and transport in hypercholesteremia and hyperlipemia	Dept. of Dermatology Tufts University School of Medicine, Boston	Dr. B. Appel Dr. W.F. Lever	1959-1961
Lipid transport, cutaneous neoplasia, biological effects of laser radiation and local chemotherapy and immunotherapy for cancers in the skin	Dept. of Dermatology Roswell Park Memorial Institute, Buffalo, NY	Dr. E. Klein	1961-1970
Local and systemic chemotherapy for premalignant, primary and metastatic neoplasms of the skin	Dept. of Dermatology Roswell Park Memorial Institute, Buffalo, NY	Dr. E. Klein Dr. O.A. Holtermann	1961-1975 1975-1983

RESEARCH EXPERIENCE (Cont'd)

Nature of Work	Department	Head of Department	Period
Systemic and local immunotherapy for premalignant and malignant lesions	Dept. of Dermatology Roswell Park Memorial Institute, Buffalo, NY	Dr. E. Klein	1961-1975
		Dr. O.A. Holtermann	1975-1983
Clinical activities of lymphokines and other non-cellular mediators of immunity	Dept. of Dermatology Roswell Park Memorial Institute, Buffalo, NY	Dr. E. Klein	1967-1975
		Dr. O.A. Holtermann	1975-1983
Chemotherapy and immunotherapy of autoimmune diseases	Dept. of Dermatology Roswell Park Memorial Institute, Buffalo, NY	Dr. E. Klein	1973-1975
		Dr. O.A. Holtermann	1975-1983

SOCIETY AFFILIATIONS

Academy of Medicine, Toronto, Ontario, Canada
Alpha Omega Alpha Medical Honor Society
American Academy of Dermatology
American Association for Cancer Research
American Association of University Professors
American College of Angiology
American Geriatrics Society
American Heart Association, Inc.
American Institute of Biological Sciences
American Medical Association
American Physicians Fellowship, Inc. for Israel Medical Association
American Society for Clinical Pharmacology and Therapeutics
American Society for Experimental Pathology
Buffalo Academy of Medicine
Buffalo-Rochester Dermatological Society
Children's Hospital Alumni Club
Children's Hospital Medical Staff Association
Dermatology Foundation
Erie County Medical Society
International Association for Comparative Research on Leukemia & Related Diseases
International Society of Experimental Hematology
International Society of Parenteral Nutrition
Medical Alumni Association, State University of New York at Buffalo
Medical Alumni Association, University of Toronto
Medical Society of the State of New York
Millard Fillmore Hospital Medical Staff Association
New England Dermatological Association
New York State Society of Dermatology
Optical Society of America
Pacific Dermatological Association
Reticuloendothelial Association
Royal Society for the Promotion of Health
Sigma Xi
Society for Cryobiology
Society for Experimental Biology and Medicine
Society for Investigative Dermatology
Transplanation Society

TEACHING EXPERIENCE

Institution	Department		Dates
Harvard Medical School	Teaching and Research Fellow Department of Dermatology	Dermatology 3rd & 4th year	1956-1960
Tufts University School of Medicine	Assistant Professor, Department of Medicine, Department of Dermatology Graduate School	Medicine 3rd & 4th year; Dermatology 3rd & 4th year	1959-1961
State University of New York	Associate Professor, Department of Pathology; Associate Professor, Department of Biochemical Pharmacology	Graduate School, Supervision of graduate students in Experimental Pathology and in Pharmacology	1962-
	Research Professor Medicine (Dermatology), Department of Medicine	Dermatology/Medicine "Clinical Biology", Introductory course in Medicine 1st year; Dermatology 2nd, 3rd and 4th medical years	1969-

RESEARCH EXPERIENCE

1946-1948

Effects of Choline Deficiency on Tissue Lipases

Under the supervision of Dr. Charles H. Best (Director, Banting Institute, Professor and Chairman, Department of Physiology, University of Toronto) and Dr. S. Hartcroft (at present Professor and Chairman of the Department of Pathology, Washington University School of Medicine) it was shown that deficiency of choline led to loss of hepatic and renal lipase activity. This loss was associated with fatty infiltration of the parenchymatous cells. These studies indicated one of the possible causes for the pathological changes produced by deficiencies of choline and related essential dietary factors.

1948-1950

Metabolic Activities of Thyroxine and Analogues

Under the direction of Dr. J.K.W. Ferguson (then Professor and Chairman of the Department of Pharmacology, at present, Director, Connaught Laboratories, University of Toronto) the actions of analogues of thyroxine were studied. Thyroxine derivatives were synthesized under the supervision of Dr. G.F. Wright (Professor of Organic Chemistry, University of Toronto). The purpose of this investigation was to prepare compounds which would inhibit or enhance one or more of the actions of the thyroid hormone. In subsequent studies it was found that several compounds related to thyroxine lowered the levels of fats, particularly cholesterol and phospholipids, in the blood.

1950-1953

Protein-metal interaction in relation to Phagocytosis

Under Dr. Edwin J. Cohn (Professor and Director, University Laboratories, Harvard University) and subsequently under Dr. Sidney Farber (Professor, Department of Pathology, Harvard Medical School, and Scientific Director, Children's Cancer Research Foundation) the interactions of metals with plasma proteins were studied. The concentrations of divalent cations were found to bear a quantitative relation to phagocytic activity. Conditions for separation, concentration, storage and transfusion of white blood cells were investigated.

1953-1956

Platelets and WBC preparations in Pancytopenia

Supervision of research program on secondary thrombocytopenia under the direction of Dr. Sidney Farber. This investigation included physical chemical studies on platelets and platelet components, studies on experimentally induced thrombocytopenia in animals and clinical investigation of patients with secondary thrombocytopenia. Clinical studies were concerned with coagulation defects and control of hemorrhage by platelet preparations. Plastic equipment was developed for the aseptic separation of blood components, permitting the preparation of platelet concentrates and white blood cell concentrates as by-products of routine blood banking or by pheresis methods. The plastic equipment facilitated the clinical exploration of transfusions of white blood cells and platelets. In this investigation it was shown in 300 patients that transfusion of platelet concentrates is a safe and potentially life saving treatment for stopping the bleeding in thrombocytopenia associated with leukemia or bone marrow depression due to chemical agents.

RESEARCH EXPERIENCE (Cont'd)

The plastic equipment which was developed for separating blood components resulted in more specific, effective and efficient transfusion therapy than had been attainable by whole blood transfusion. The separation methods permitted removal of the specific component needed by a particular patient, thus reducing the potential complications of whole blood transfusions and eliminating the unnecessary loss of blood constituents. The remainder of the blood was therefore available for other patients. Alternately, the red blood cells could be returned to the donor who could then donate blood more frequently.

1953-1956

Interactions of synthetic polypeptides in biological systems

Studies on interactions of synthetic polypeptides in biological in vitro systems and in vivo were carried out under the direction of Dr. S. Farber in association with Dr. E.R. Blout (at present Professor and Chairman, Department of Biological Chemistry, Harvard Medical School) in the course of the development of blood volume expanders. These studies were undertaken to provide synthetic substitutes for plasma proteins in view of the shortage of whole blood and plasma for the treatment of shock due to blood loss. The feasibility of developing safe substitutes for this purpose was demonstrated.

1956-1961

Lipoprotein metabolism and transport

In association with Dr. W.F. Lever (then Assistant Professor, Department of Dermatology, Harvard Medical School, at present, Professor and Chairman, Department of Dermatology, Tufts University School of Medicine) studies on normal lipid transport and its disturbances in patients with primary and secondary forms of hyperlipemia and of hypercholesteremic xanthomatosis were carried out. These diseases of fat metabolism, which are characterized by high blood levels of cholesterol and other lipies, are associated with degenerative changes of the blood vessels and the heart, and with deposition of fat in the skin and subcutaneous tissues. The relation, however, between disturbed fat metabolism and the pathological changes in the skin and blood vessel is not understood.

It was demonstrated that the defective lipid metabolism was associated with abnormalities of the lipoproteins. Further clarification of the nature of the defects required studies on puron purified components of the systems, by which fats are carried in the blood. These studies included purification and characterization of lipases. The kinetics of these enzyme activities were investigated. The in vitro action of purified lipases on beta-lipoproteins was observed to result in the formation of low Sf classes. Lipases were thus shown to reduce the large molecular weight liproproteins in hyperlipemic blood to liproproteins of the lower molecular weight range, usually present in normal blood.

1961-1970

Investigation of lipid transport

The investigation on lipid transport is a continuation of previous studies. Pancreatic lipase of human and bovine origin was separated and purified. The presence of cofactors in human, porcine, and bovine pancreatic lipase was demonstrated. The cofactor

RESEARCH EXPERIENCE (Cont'd)

preparations obtained from human, porcine, and bovine sources were shown to be interchangeable in restoring lipase activity to the respective apo-enzymes. In vitro incubation of pancreatic lipase with lipoproteins was found to alter the distribution of the components of the alpha and beta-lipoproteins on analytical ultracentrifugation. This effect was considerably more marked when triglycerides were added to the incubation mixture. Components of the alpha lipoprotein fraction were shown to act as free fatty acid acceptors. It was further shown that glycerol phosphatides can inhibit the release of free fatty acids from triglycerides by lipases. Phosphatides may thus act as regulators of transport, utilization, and storage of fatty acids.

1961-1970

Interaction of laser radiation with biological systems

Studies on interaction of laser radiation with biological systems were carried out in association with Dr. S. Fine (Profes-or and Chairman, Department of Bio-medical Engineering, Northeastern University). Interactions of high intensity electromagnetic radiation with biological systems were shown to produce (in addition to heat per se) phase transformations, pressure and possibly, shock waves, secondary electromagnetic radiation, sonic, hypersonic and ultra-sonic frequencies, charged particles including free radicals, and high electric field gradients. Laser irradiation of proteins in vitro resulted in quantitative changes of biological activities without detectable conformational changes. Differential effects of laser radiation on pigmented and non-pigmented biological material were demonstrated in vitro and in vivo. Laser irradiation was shown to induce regressions of several experimental tumors. Thresholds for production of minimal lesions and for fatal injuries were determined in intact animals. Hazards of laser radiation were investigated and a safety program was outlined. Assessment of potential hazards and studies on mechanisms of interactions were carried out as a basis for clinical applications of laser radiation.

1961-

Chemotherapy for Cutaneous Tumors

Studies on neoplasms in the skin include evaluation of direct (local) administration of cytostatic agents to tumors, investigation of mechanism of action and exploration of host response. The accessibility of skin tumors and some of their other properties render them particularly suitable as model systems for studies of neoplasia. Data indicate selective (chemical) action on tumors with minimal effects on adjacent normal tissues, resulting in lasting resolution of basal cell carcinomas and premalignant (solar) keratoses. These studies were based on statistically significant ($p > 0.001$) data and were carried out on more than 100 patients with an aggregate of more than 5000 individual precancerous lesions or tumors. Topical chemotherapy was shown to be effective for the management of skin cancer in which surgery or radiation therapy is complicated by the involvement of large areas. Selective reaction of neoplasms to topical chemotherapy permits recognition of skin tumors and precancerous lesions before

RESEARCH EXPERIENCE (Cont'd)

they are otherwise detectable and aids in reducing the incidence of skin cancer. These studies were subsequently extended to 22 Institutions.

1961-

Immunotherapy for skin cancer

In the studies on local chemotherapy several chemical agents were found to induce cutaneous hypersensitivity. These reactions were considerably more intense in epidermal neoplasms (basal cell carcinoma, squamous cell carcinoma in-situ, solar and arsenical keratoses, leukoplakia) than in the normal tissues. After hypersensitivity had been induced, several of these agents were shown to produce an accelerated reaction of the delayed hypersensitivity type which resulted in resolution of the neoplastic lesions with minimal or no untoward effects on normal skin. Decrease of the challenging dose by 2 to 3 orders of magnitude (e.g. 5 parts/1,000,000) below the sensitizing dose (e.g. 5/1,000 to 5/10,000) limited the immune reaction to neoplasms. These studies indicated the potential for a qualitatively and quantitatively differential reaction in normal and neoplastic tissues respectively. The usually adverse allergic type of reaction may therefore be utilized therapeutically by lowering the challenging dose, thus providing a therapeutically adequate index. This approach was explored by systemic administration of the challenging dose without generalized allergic manifestations.

We have shown that immune challenge reactions to cutaneous sensitizing agents (Dinitrochlorobenzene - DNCB, 2,3,5-Tri-ethylene-imino-1,4-benzoquinone - TEIB) result in more intense effects on epidermal cancers and premalignant lesions than in the normal skin. After induction of hypersensitivity the skin is exposed to the sensitizing agent at a concentration considerably below that required to elicit a delayed hypersensitivity reaction in normal skin. Neoplastic lesions, but not the surrounding normal skin, develop an intense reaction and are eradicated.

1967-

In Vitro Studies on tumor immunotherapy

Studies were carried out in vitro and in animal models to elucidate the mechanism of selective immune effects resulting in tumor eradication. We showed that tumor cells are killed by in vitro exposure to autologous leukocytes of sensitized patients when the sensitizing agent is added. Components of sera of inbred rats with (polyoma) virus induced tumors were shown to stimulate in vitro cell destruction by peripheral (peritoneal) leukocytes of syngeneic animals.

Subcutaneous administration of peritoneal leukocytes of DNCB sensitized guinea pigs induced local passive transfer of sensitivity in mice. Challenge following local passive transfer was blocked by local injection of anti-DNCB antibody.

Challenge with DNCB prevented chemical induction of skin cancers, but not of papillomas in sensitized mice. Discontinuation of

RESEARCH EXPERIENCE (Cont'd)

DNCB of chemically-induced skin cancers in sensitized mice resulted in regression of tumors.

Challenge responses to DNCB were not prevented by concurrent local administration of high concentrations of anti-mitotic agents.

Transfer of immunity was followed by eradication of skin cancers as a result of immune challenge. The nature of the donor's tumors did not effect the response. Challenge reactions following local passive transfer of hypersensitivity (DNCB, TEIB) were considerably more marked in skin tumors and lymphoma infiltrates than normal skin and resulted in regressions.

1962-

Clinical immunotherapy for other tumors located in the skin

Our studies on tumors in man showed that haptene induced hypersensitivity produces selective anti-tumor effects in cutaneous lymphomas and metastatic cancer.

Selectivity of immune challenge could be augmented. Concurrent challenge with multiple sensitizers augments the selective effects on tumors. Local administration of high concentrations of antimitotic chemicals to tumor sites under immune challenge enhances rather than inhibits selectivity of anti-tumor effects. Resistance against anti-tumor effects of delayed hypersensitivity challenge reaction does not develop when challenge is repeated intermittently over periods of up to 7 years.

Intractable multiple cancers and precancerous lesions of the skin eradicated by immune challenge showed less than 5% tumor recurrences in 90 patients on 1-7 year follow-up. Selective response to immune challenge reveals otherwise undetectable neoplasms. Incidence of tumors was markedly reduced in xeroderma pigmentosum following whole body immune challenge.

Immune challenge resulted in selective reactions and regressions of lesions of reticulum cell sarcoma and mycosis fungoides. Challenge of single lesions in mycosis fungoides produces reactions in other unchallenged lesions. In immuno-deficient patients unable to develop new hypersensitivity, challenge based on immunologic memory (e.g. PPD) results in eradication of epidermal or mycosis fungoides tumors. Malignant melanomas converted to benign "halo nevi" followed by resolution during maintenance of immune challenge.

During the past ten years we demonstrated that the immune mechanism can be controlled and used for the prevention and cure of cancer in animals and man. Immunotherapy for cancers and precancerous lesions was developed which resulted in cures of more than 90% of lesions, lasting longer than five years. These results were obtained in a group of more than 100 patients with extensive malignant disease of the skin involving up to 50% of

RESEARCH EXPERIENCE (Cont'd)

the body surface, who could not be adequately treated by other methods. Patients who had required from 50-100 surgical procedures per year have been maintained on immunotherapy for up to seven years without need for surgery. We further demonstrated that immunotherapy results in the prevention and early diagnosis as well as in cures of skin cancer. In addition to being a practical life-saving procedure for severe skin cancer, the immunologic approaches developed by us have provided suitable model systems for studies in tumor biology and basic immunology.

1962

Clinical immunotherapy for accessible Primary and secondary malignant lesions in the skin

Our work shows that control of cancer by immune mechanisms is primarily exerted through specific cell-mediated immunity. When immunity is transferred to or adopted by another patient, it was shown to be effective for the treatment of malignant lesions. We further showed that specific cell-mediated immunity under standardized conditions can be stimulated to result in highly reproducible (curative) effects on malignant disease. The principles of immunotherapy have been successfully extended by us and others to mycosis fungoides and other lymphomas, and to metastatic lesions of other types of cancer. These approaches were subsequently extended to melanomas, lymphomas, breast cancer, and sarcomas indicating general underlying principles.

1967

Lymphokines and other non-cellular mediators in tumor immunology

Newly or previously acquired immunity (immune memory) can be utilized for cancer therapy. Local immune reactions can be generalized systemically to result in resolution of disseminated malignant tumors. Immunity transferred by white blood cell preparations from responsive to non-responsive patients (i.e. impaired immunocompetence) can be used for immunotherapeutic procedures. Concurrent or sequential combinations of immunotherapy, cancer chemotherapy and/or surgery have been shown to be effective when single treatment methods fail. Separated components (lymphokines, macrophages) of immune antitumor reactions are being investigated in cancer patients to amplify inadequate immune responses.

1978

Chemotherapy for augmenting cell mediated immunity

The most recent clinical studies have been in the area of selective inhibition of subpopulations of lymphocytes, particularly suppressor I lymphocytes by systemic administration of exceedingly low doses of antimitotic agents. In the course of these studies, the compromised immunocompetence of patients with malignant, autoimmune and other serious disease were distinctly augmented. Marked therapeutic effects were noted in a number of patients with malignant diseases when low doses of antimitotic agents were combined with topical immunotherapy. Complete, but temporary, control of pemphigus vulvaris was induced employing low doses of single or multiple antimitotic agents, while patients with vasculitis and those with lymphomatoid papulomatosis were brought into at least partial maintained remissions. Observations were further made which showed significant therapeutic effects in two patients, each with a different genetic disease (Ichthyosis Linearis Circumflex-ILC: Rothmund Thompson Syndrome-RTS).

CONTRIBUTIONS TO BOOKS AND MONOGRAPHS

Surgenor, D.M., Tullis, J.L., Batchelor, W.H. and Klein, E.: Interaction of proteins with calcium and barium ions. In: Blood Cells and Plasma Proteins. Their State in Nature. J.L. Tullis, Editor. Memoirs of the University Laboratory of Physical Chemistry Related to Medicine and Public Health, Harvard University. Academic Press, Inc., N.Y., Vol. 2, p. 43, 1953.

Surgenor, D.M., Tullis, J.L. and Klein, E.: Interactions of plasma proteins with leukocytes. In: Blood Cells and Plasma Proteins. Their State in Nature. J.L. Tullis, Editor. Memoirs of the University Laboratory of Physical Chemistry Related to Medicine and Public Health, Harvard University. Academic Press, Inc., N.Y., Vol. 2, p. 50, 1953.

Klein, E.: The Platelet Count. In: Syllabus of Laboratory Examinations in Clinical Diagnosis. L.B. Page and P.J. Culver, Editors, Harvard University Press, Cambridge, Mass., 1960.

Fine, S. and Klein, E.: Laser. In: McGraw-Hill Yearbook of Science and Technology, pp. 222-229, 1966.

Fine, S. and Klein, E.: Ultraviolet Lasers. In: The Biologic Effects of Ultraviolet Radiation (with emphasis on the skin). F. Urbach, Editor. Pergamon Press, New York, NY, pp. 115-123, 1969.

Klein, E.: Immunotherapy of Cutaneous Neoplasms. In: Skin Surgery. Ervin Epstein, M.D., Editor. Charles C. Thomas, Publisher, Springfield, Ill., pp. 324-341, 1970.

Klein, E., Stoll, H.I., Milgrom, H., Helm, F., Walker, M.J.: Tumors of the Skin. XII Topical 5-Fluorouracil for Epidermal Neoplasms. In: Symposium on Recent Advances in the Management of Skin Neoplasms. Klein, E., Coordinator. Published as a single issue of the Journal for Surgical Oncology, Vol. 3, No. 3., 1971. G. Murphy, Ed., Plenum Press.

Klein, E., Milgrom, H., Stoll, H.L., Jr., Helm, F., Walker, M.J. and Holtermann, O.A.: Topical 5-Fluorouracil Chemotherapy for Premalignant and Malignant Epidermal Neoplasms. In: Cancer Chemotherapy II, The Twenty-Second Hahnemann Symposium. I. Brodsky, S.B. Kahn, and J.H. Moyer, Editors. Grune and Stratton, New York, N.Y., pp. 147-166, 1972.

Klein, E.: Chemotherapy and Immunotherapy for Cancer Involving the Skin. In: Proceedings of the Seventh National Cancer Conference. J.B. Lippincott Co., Philadelphia, Pa., pp. 567-578, 1973.

Klein, E.: Progress in Immunotherapeutic Approaches to the Management of Neoplasms. Chapter IV. In: Perspectives in Cancer Research and Treatment. G.P. Murphy, Editor. Alan H. Liss, Inc., New York, N.Y., pp. 51-58, 1973.

Klein, E., Burgess, G.H. and Helm, F.: Neoplasms of the Skin. In: Cancer Medicine. J.F. Holland and E. Frei, III, Editors. Lea and Febiger, Philadelphia, Pa., pp. 1789-1822, 1973.

CONTRIBUTIONS TO BOOKS AND MONOGRAPHS (Cont'd)

Klein, E., Papermaster, B.W., Case, R.W. and Apisarnthanarax, P.: Immunological Aspects of Neoplasia. In: Immunological Aspects of Neoplasia. (A collection of papers presented at the 26th Annual Symposium on Fundamental Cancer Research, 1973, at the University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Texas) Williams and Wilkins, Baltimore, Md., pp. 549-578, 1975.

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Edmund Klein (1921-1999)

Edmund Klein, MD, a dermatologist and pioneer in cancer immunotherapy who received the highest award in American medicine, the Lasker Award, died of complications of diabetes mellitus and congestive heart failure on July 24, 1999, in Buffalo, New York, at the age of 77 years. The son of a Viennese cantor, Dr Klein parlayed an acceptance letter at an English high school into a British visa, allowing his timely departure from Vienna as a 17-year-old secondary school student shortly after the Anschluss. After entering England without money, means of support, or a place to reside, he successfully obtained sponsorship so that his sister could flee as well, but was unable to help his doomed parents. This Viennese-born, British-, Canadian-, and American-educated physician received an amazing total of 36 scholarships for academic proficiency. He was elected to the Alpha Omega Alpha Honor Society in 1949 at the University of Toronto Medical School, where he began his academic medical research career under the supervision of Charles H. Best (co-discoverer, with Banting, of insulin).

After further research and clinical training with Sidney Farber, Walter F. Lever, and others at Harvard Medical School (1951-1959),[1-4] where Ed also completed a residency in dermatology at Massachusetts General Hospital (1956-1959), he was appointed assistant professor of dermatology and medicine at Tufts University School of Medicine in 1959. With strong encouragement from Julian L. Ambrus MD, PhD, he succeeded another European refugee, Frederick Urbach, MD, at Roswell Park Memorial Institute (RPMI) in Buffalo. In 1961 he became research professor and chairman of its Department of Dermatology, where he continued his distinguished career for more than a quarter century alongside a worthy academic dermatologic faculty, including Howard L. Stoll, Jr, MD, Frederick Helm, MD, Halina Milgrom, MD, Ole A. Holtermann, MD, PhD, Jacob E. Berger, MD, Gordon H. Burgess, MD, John T. Crissey, MD, Herbert L. Traenkle, MD, and Yona Laor, MD. Nondermatologic colleagues included Ben W. Papermaster, PhD, Robert W. Case, Pharm B, Clara M. Ambrus, MD, Julian L. Ambrus, MD, Audrey Fjelde, PhD, and many others, as well as his

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patient care, passing the boards, or doing well on in-service examinations? Does this foster—or unintentionally discourage—sound lifelong reading habits? Aren't there other goals, more enlightened and more enlightening, that we should consider? Plutarch's adage "The mind is not a vessel to be filled but a fire to be kindled" comes to mind.

As an Assistant Editor, I would be proud if every article published in the Journal were novel, interesting, and important—in other words, if every article were both readable and worth reading. (I'd also like it if every article were eloquent, funny, and short.) The Editors would love to receive manuscripts that are perfect when first submitted, but these papers probably don't exist. The peer review system is intended to select the most worthwhile papers and nudge them along toward that elusive perfection. Occasionally reviewers and editors err in their selections and sometimes they don't nudge hard enough. We acknowledge these lapses but also remind the readers to be selective in what you read and skeptical in what you believe.

The best way to produce a well-written paper is to start with a well-designed study. Consult a statistician before conducting the study to decide how to collect, analyze, and present data. Review Strunk and White's *The Elements of Style* before composing the paper. Remember that a straightforward unadorned writing style has its own elegance. Draft your paper, revise it a few times, enlist others to criticize it, and then revise it a couple more times. Repeat as necessary. Oh, and here's a tip to get the reviewers on your side: follow the Instructions for Authors. (There are some adages, true or not, that we can't shake: "Clear writing is the product of clear thinking" and "Adherence to the Journal's Instructions means, well, it means a lot.")

The peer review and editorial processes work well—and we strive to improve them further, but they will never be infallible. So until you announce that all articles in the Journal are perfect (either submitted that way or nudged there), you should be selective in your reading. The corollary is that we shouldn't require your residents to read indiscriminately. Let's imbue in our residents an appreciation of science, hone their curiosity and skepticism, and foster their inclinations to contribute to the corpus of biomedical knowledge. Maybe we can do this with clearly written papers that have good study designs and relevant messages. In turn, residents must supply the tinder for Plutarch's fire in the form of intellectual inquiry and must acquire the skills to read worthy papers in a critical manner.

We do not live in a world where unhappy articles, like Tolstoy's unhappy families, have tales worth telling.

Scott A. Norton, MD, MPH
Assistant Editor

long-time faithful administrative assistants Terri Legierski and Marlene E. Merzacco. All were inspired by his contagious scientific vigor and eventually contributed in major ways to dermatology and cancer research. RPMI at that time was an extraordinary milieu, America's first institute devoted entirely to cancer research: an inspiring and dynamic academic center that was an independent graduate school unit of the State University of New York at Buffalo situated directly across the street from the State University of New York Buffalo School of Medicine's main teaching hospital, Buffalo General Hospital.

Dr Klein's innovative contributions led to new concepts and new life-saving treatment methods,[1-6] some still in wide use today for leukemic children[1-3] and as immunotherapy for adults with skin cancer.[7-19] Dr Klein along with Dr Isaac Djerassi introduced the modern separation, storage, and transfusion techniques for blood components, allowing the transition from whole blood to the use of separated and concentrated life-saving blood components.[1-3] But Klein branched out further, making additional lasting marks, particularly in immunotherapy. A distinguished physician from the National Institutes of Health observed, "Clinical immunotherapy owes its rebirth in part to Klein's stubborn pursuit of his observations and their implications despite the ridicule and disbelief of many of his colleagues."[20] "In all fairness he was a genuine founder of cancer immunotherapy," Isaac Djerassi recently reflected. Dr Klein earned many honors, including the First Prize for Originality of Research from the International Society for Hematology in 1956, the Lasker Award in 1972, and The Founders Award in Cancer Immunology in 1975. His 1986 award from the American Society for Laser Medicine and Surgery honored him for being the first to introduce lasers into biomedical research,[5,6] working in animal models before others did so in humans.

In summary, Dr Edmund Klein's accomplishments included the following:

1. The invention with Dr Djerassi of the closed systems of plastic bags for the sterile separation of whole blood into its components of plasma, red blood cells, platelets, and white blood cells. This discovery, in time, revolutionized completely the field of blood transfusion, replacing the ubiquitous transfusion of whole blood with the administration of the specific deficient blood components, such as red blood cells for anemia, platelets for thrombocytopenia, plasma for decreased blood volume, and leukocytes for leukopenia. This permitted a much more efficient utilization of human blood with one donation helping at least 3 different patients instead of one. This separation of blood components made possible the treatment of thrombocytopenic hemorrhage with infusion of platelet concentrates, which would have been impossible with whole blood because of the volume limitations. Platelet transfusions, on the other hand, made all cancer chemotherapy possible by removing the risk of fatal hemorrhages due to the thrombocytopenia resulting from the chemotherapy.[1-4]

2. The first biomedical research on the effects of lasers working in animals with Samuel Fine, before others did so in humans.[5,6]

3. Local antitumor chemotherapy for neoplastic cutaneous lesions,[7-11] for which he received the Lasker Award. He developed topical 5-fluorouracil therapy, an anticancer treatment still approved by the Food and Drug Administration and available commercially.

4. Discovering the value of immunotherapy for cutaneous cancers and thus pioneering modern immunotherapy.[12-18] He introduced local immunotherapy for cure of cancers and premalignant growths of the skin and accessible mucosa. This was the first demonstration that the immune defense system could be stimulated to control cancer.

5. Early work in clinical exploration of lymphokines in patients with neoplastic disease,[17,18] which led to today's preeminence of cytokines and interleukins. He first demonstrated that administration of lymphokines to accessible tumors in humans can result in regression of malignant diseases.

6. Devising low-dose vinblastine therapy for Kaposi's sarcoma, one of the earliest effective treatment methods for this neoplasm.[19]

Edmund Klein was an amazing person. His interests were legion. He worked long, and sometimes very odd, hours. The Editor of this Journal first met him at 1 o'clock in the morning when he was in the middle of an experiment as a summer student at RPMI and Dr Klein was just getting to work. That meeting was the initial impetus for Dr Bernhard's interest in dermatology. Klein was a gracious and gifted teacher and mentor of aspiring physicians. His RPMI summer program undergraduate trainees included Steven R. Parmett[18] and Jeffrey D. Bernhard,[15,16,18] who both went on to academic careers, the latter as professor and director of dermatology at the University of Massachusetts Medical School. Similarly, Ed inspired dermatology residents, including Charles E. Vickerman, Jr, MD, Arthur P. Birnkrant, MD, Prapand Apisarnthanarax, MD, Mohammed Yaqub, MD, Patrick G. W. Kenny, MD, Bernard F. McEvoy, MD, Robert A. Schwartz, MD, MPH, and Frederick Helm, MD. The latter two also became professors and heads of dermatology: Schwartz at the New Jersey Medical School and Helm at the State University of New York School

of Medicine at Buffalo. Helm was Ed's first resident as Dermatology Department Chairman, having come from Boston with Ed in 1961.

Dr Klein was revered by his patients, with inevitable and often lengthy delays because of the time he spent with each, sometimes deep in thought, sometimes kibitzing late into the night. He enjoyed his association with Boston and its academic and political establishment and was pleased to be Guest Professor of Biomedical Engineering at Northeastern University in Boston, and a consultant at Harvard's Dana Farber Cancer Institute. He was called to testify on several occasions in support of cancer research funding before the US Congress and was a respected member of numerous governmental advisory committees addressing health care and cancer research issues, including the National Advisory Council on Health Care Technology of the Department of Health and Human Services. To Ed Klein "cancer" was an adversary against which he could labor, chain-smoking and drinking black coffee day and night, insistent that he had an ideal battlefield, the skin and accessible mucosa, where malignancies were readily available for clinical observation and intervention. He was proud of his 3 daughters, Judith Augustino (a nurse), Rene Rubino (in public relations), and Amy Szymoniak (an attorney) and two sons, Lawrence Klein (MD, Dartmouth University School of Medicine) and Peter Klein (MD, Johns Hopkins University School of Medicine). Larry and Peter followed in their father's footsteps into academic medicine, the former as a dermatologist and dermatopathologist at the University of South Carolina, the latter as an internist at the University of Pennsylvania. He is also survived by his wife of 49 years, Martha Doble Klein, and their 9 grandchildren.

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EDMUND KLEIN, M.D. (1921-1999)

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OBITUARY

EDMUND KLEIN, M.D. (1921-1999)

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Edmund Klein, MD recipient of the highest award in American Medicine, the Lasker Award for clinical research in cancer immunology, died on July 24, 1999 in Buffalo, New York of complications of diabetes mellitus and congestive heart failure at the age of 77 years. The dynamic son of a prominent Viennese scholar and cantor, Ed narrowly escaped to England as a 17-year-old secondary school student shortly after the Anschluss. Entering England with no money, means of support and no place to live, he was able to help his sister to flee as well, but unable to convince his doomed parents to do so. This Viennese born (October 22, 1921), British, Canadian (B.A., M.D., University of Toronto, Classes of 1947 and 1951) and American educated (hematology and dermatology, Harvard Medical School) professor began his academic research career under the supervision of Charles H. Best (co-discoverer, with Banting, of insulin), Director of the Banting and Best Institute. After further research and clinical training with Sidney Farber and others at the Harvard Medical School (1951-1959), where he also completed a residency in dermatology (1956-1959), he was appointed in 1959 as assistant professor of medicine and dermatology at Tufts University

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School of Medicine. With strong encouragement by one of us (JLA), he was recruited as Fred Urbach's successor at Roswell Park Memorial Institute in Buffalo, and began in 1961 as research professor and chairman of its Department of Dermatology, where he continued his distinguished career for more than a quarter century.

Dr. Klein's major contribution in the biomedical sciences over the past forty years have led to new concepts and new life-saving treatment methods, which have come into wide use. He also published in related and other fields of Medicine. Terry (1976), summarizing some of Ed Klein's accomplishments stated that Klein was the "Father of Modern Immunotherapy." Terry observed "Clinical immunotherapy owes its rebirth in part to Kleins's stubborn pursuit of his observations and their implications despite the ridicule and disbelief of many of his colleagues." Dr. Klein earned the Lasker Award in 1972 and The Founders Award in Cancer Immunology in 1975. His 1986 award from the American Society of Laser Medicine and Surgery honors Dr. Klein for being the first to introduce lasers into biomedical research. Honors and awards were frequent from his student days too. He was not only elected to the Alpha Omega Alpha National Honor Medical Society in1949 as a medical student, but he received an amazing total of thirty-six scholarships for academic proficiency.

1. We summarize Dr. Klein's accomplishments below. His major publications are referred to at the end.

Dr. Klein introduced blood cell separation techniques (platelet concentrates, white blood cell concentrates) for the treatment of patients with malignant diseases and blood dyscrasias. The introduction of platelet transfusions to prevent fatal hemorrhages in children with acute leukemia and other malignant diseases.

1. He showed the use of concentrated platelet transfusions to control bleeding caused by anti-cancer drugs, thus permitting wider use of cancer chemotherapy.

Development of the first practical method for the separation of concentrated white blood cell preparations for the treatment of otherwise fatal infections.

2. Development of methods for the large-scale procurement and separation of human blood components.

Introduction of cytopheresis to obtain platelets and white blood cells in virtually unlimited amounts, by returning red blood cells to the donor.

3. Introduction of lasers into biomedical research leading to the first studies on the biological effects of lasers.

4. Introduced local antitumor chemotherapy for neoplastic lesions in the skin.

Developed topical 5-fluorouracil and related anticancer agents.

Introduction of topical chemotherapy as a treatment and cure for cancers and precancerous growths of the skin and accessible mucosa.

5. Devised low dose vinblastine therapy for Kaposi's sarcoma, one of the earliest effective treatment methods for this tumor in patients with AIDS.

6. Pioneered modern immunotherapy.

Introduction of local immunotherapy for cure of cancers and premalignant growths of the skin and accessible mucosa.

This was the first demonstration that the immune defense system can be stimulated to control cancer.

7. Introduced clinical exploration of lymphokines in patients with neoplastic disease.

First demonstration that the administration of lymphokines to accessible tumors in man can result in regressions of malignant diseases.

There was more to Ed Klein, the man, than the accomplishments listed above. We will never forget watching him evaluate patients at almost midnight, speaking with them while leaning upon his glass covered Salvador Dali masterpiece stretched out on his consultation room desk. He was revered by his patients, with inevitable delays due to the time he spent with each. His clinical acumen and determination in tackling seemingly hopeless cases encouraged referrals from around the world. He enjoyed his association with Boston and its academic and political establishment, flying back often. He was pleased to be Guest Professor of Biomedical Engineering at Northeastern University in Boston, and to be a consultant at Harvard's Dana-Farber Cancer

Institute. Nevertheless, he remained grateful to Canada for giving him a home when he arrived as a penniless young man in 1942, and declined to forsake his Canadian citizenship despite the personal and professional advantages in doing so. An impressive example was his unwillingness to join the highly prestigious three member President's Cancer Advisory Panel, because it required American citizenship and therefore the renouncing of his Canadian citizenship. However, he was called to testify on several occasions in support of cancer research funding before the Congress of the United States, and was a respected member of numerous governmental advisory committees addressing health care and cancer research issues, including the National Advisory Council on Health Care Technology of the Department of Health and Human Services.

He was pleased that three of his students, Jeffrey D. Bernhard, Frederick Helm and Robert A. Schwartz became professors and heads of dermatology: Bernhard at the University of Massachusetts, Schwartz at the New Jersey Medical School and Helm at the State University of New York at Buffalo.

He was proud of his five children, Lawrence Klein (a dermatologist and dermatopathologist at the University of South Carolina), Judith Augustino (a nurse), Peter Klein (an internist at the University of Pennsylvania), Rene Rubino (in public relations), and Amy Szymoniak (a lawyer). He is survived by them and by his wife of 49 years, Martha Doble Klein, and their nine grandchildren.

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